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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,538	09/29/2003	Shimin Liu	N12-001	1846

26813 7590 02/22/2006

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,538	LIU ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 22-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-4* is/are allowed.

6)☒ Claim(s) *1,5-7,9-19 and 22-34* is/are rejected.

7)☒ Claim(s) *8 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. In response to the amendment filed on February 1, 2006, prosecution in the instant application is being re-opened in order to institute the following new grounds of rejection.

2. Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 5 of claim 31, the phrase "the treated specimen" lacks antecedent basis.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1, 5-7, 9-14, 18 and 22-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz (US Patent no. 4,378,971).

Schwartz teaches of a method and apparatus for quantitatively determining the level of hemoglobin in a biological sample. The method is used for diagnosing diseases in an individual such as intestinal tumors (see lines 24-26 in column 1 of Schwartz), and is used as an occult blood assay (see lines 57-59 in column 1 of Schwartz). The method comprises the steps of collecting a biological sample such as feces or urine, and combining the sample with a reacting solution specific for heme compounds such as hemoglobin. Schwartz teaches that if the sample is a feces sample, the sample should be homogenized in a saline solution. See lines 50-51 in column 8 of Schwartz. The reacting solution contains a strong reducing agent or salt. Schwartz teaches that the strong reducing agent is preferably ferrous oxalate or ferrous sulfate, but also indicates that other reducing agents may be used. See lines 37-48 in column 5 of Schwartz. The reducing agent causes the heme portion of hemoglobin to be converted to porphyrin. During the conversion reaction, iron is removed from the non-fluorescing heme-containing porphyrin, resulting in the iron-free fluorescing protoporphyrin, which fluoresces red upon exposure to ultraviolet light at a wavelength of approximately 408-410 nm. Therefore, the removal of the iron from the porphyrin molecule in heme forms a porphyrin-like fluorescing compound, i.e. protoporphyrin. See lines 25-58 in column 6 of Schwartz. The protoporphyrin fluoresces with a spectrum from about 500-700 nm. See lines 7-23 in column 8, lines 40-42 in column 13 and lines 3-5 in column 14 of Schwartz. The fluorescence of the sample is then measured with a fluorimeter or spectrofluorophotometer. See lines 41-43 in column 7 of Schwartz. Schwartz

teaches that the fluorescence not related to the heme compound reaction in a biological sample must be removed from the sample in order to obtain an accurate measurement of the amount of hemoglobin or blood in a sample. See lines 55-68 in column 2 and lines 1-8 in column 3 of Schwartz. The measured fluorescence is compared with standard known levels of hemoglobin or protoporphyrin concentrations, and the concentration of the heme compounds or hemoglobin in the biological sample is calculated. Schwartz also teaches of a kit to be used in performing the method. The kit comprises a structure 18 having a plurality of reaction chambers 19a, 19b, 20a and 20b therein. These reaction chambers are provided with a cap 21 and a transparent window 22 that enables fluorescence of the material in the chambers to be assayed. Some of the chambers contain a reaction solution comprising a reducing agent. Biological test samples are then added to each of the chambers, where any heme compounds in the samples are reduced to a fluorescent protoporphyrin compound. Other of the chambers contain a non-reducing solution to serve as blank chambers that measure only naturally occurring fluorescence in a test sample. It is inherent in the kits taught by Schwartz that they contain instructions and protocols to be used with the components of the kit in order to perform a certain method, i.e. a method of determining blood products in a biological sample. See lines 61-68 in column 9 and lines 1-63 in column 10 of Schwartz.

Schwartz fails to teach that the fluorescent biological specimen is excited with light at "about 480 nm". However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to excite the fluorescent biological sample being analyzed for blood taught by Schwartz with light at about 480 nm since Schwartz teaches that the biological sample is excited with light at about 410 nm, and both 410 nm and 480 nm are in the blue visible light

region of the electromagnetic spectrum. Therefore, the teaching of Schwartz renders the instant claims obvious since the specimens both in the instant claims and in Schwartz are treated with a reducing agent, both specimens fluoresce with a spectrum in the same range (i.e. 500-700 nm), and both specimens are excited with light in the same region of the electromagnetic spectrum (i.e. between 400-500 nm). In the absence of unexpected results, an excitation wavelength of about 410 nm taught by Schwartz can be read as "about 480 nm" since both wavelengths fall within the same region of the electromagnetic spectrum.

Schwartz also fails to teach that the directions of the kit instruct one to excite a biological specimen at about 480 nm so that the specimen fluoresces from about 530 nm to about 670 nm. It is noted that the fluorescence limitations in the instant kit claims do not serve to limit the physical components of the kit, and therefore, are not given patentable weight. In addition, the printed instructions recited in the instant kit claims merely teach a new use for an existing product taught by Schwartz. It has been held that the addition of new printed instructions to a known product or kit does not render the product patentable. See In re John Ngai and David Lin (Fed. Cir. May 13, 2004).

Schwartz also fails to teach that the biological specimen analyzed for the presence of blood can be cerebral tissue microvasculature. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the method taught by Schwartz to detect the presence of blood in cerebral tissue microvasculature since the method taught by Schwartz has the ability to detect blood in a biological sample where blood is not normally supposed to be (i.e. feces or urine), and therefore, one of ordinary skill in the art would expect

that the known phenomenon of bleeding in the brain could be detected by applying the method taught by Schwartz to cerebral tissue samples.

Schwartz also fails to teach that the reacting solution contains saline therein, fails to teach that the method can be used to detect erythrocytes in a sample, and fails to teach of purifying a fecal sample before reacting the sample with the reducing agent. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to include saline in the solution of reducing agents taught by Schwartz since saline is disclosed by Schwartz as being used for homogenizing a fecal sample, and the inclusion of saline in the solution of reducing agents would avoid having to separately homogenize a fecal sample, and would allow a single solution to facilitate both the homogenization of a fecal sample and the reduction of the porphyrin molecules therein. It also would have been obvious to one of ordinary skill in the art to realize that the method taught by Schwartz can be used to detect erythrocytes in a biological sample since Schwartz teaches that the method is used to determine hemoglobin and heme compounds in a sample, and erythrocytes are well known as containing hemoglobin therein. Therefore, when hemoglobin is detected using the fluorescence method taught by Schwartz, erythrocytes in the sample are also inherently detected since hemoglobin originates from erythrocytes. It also would have been obvious to one of ordinary skill in the art to purify fecal samples collected in the method taught by Schwartz in order to remove materials that might interfere with the production of an accurate fluorescence measurement since Schwartz teaches that fecal samples contain substances therein that produce fluorescence that is not related to the heme compound. By purifying the fecal samples, these compounds would be removed to obtain a value for fluorescence that is due specifically only to the porphyrin-like compounds formed from heme.

7. Claims 14-17, 19, 22-25, 31 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomita et al (US 2004/0171016).

Tomita et al teach of a kit containing sodium borohydride, a strong reducing agent. See claims 16, 18 and 20 in Tomita et al. The kit also inherently contains printed instructions therein for performing a certain method using the strong reducing agent as well as other reagents and containers for holding the reagents.

Tomita et al fail to teach that the directions of the kit instruct one to excite a biological specimen at about 480 nm so that the specimen fluoresces from about 530 nm to about 670 nm. It is noted that the fluorescence limitations in the instant kit claims do not serve to limit the physical components of the kit, and therefore, are not given patentable weight. In addition, the printed instructions recited in the instant kit claims merely teach a new use for an existing product taught by Tomita et al (i.e. a kit containing the strong reducing agent, sodium borohydride). It has been held that the addition of new printed instructions to a known product or kit does not render the product patentable. See In re John Ngai and David Lin (Fed. Cir. May 13, 2004). Therefore, the kit taught by Tomita et al renders obvious the kit recited in instant claims 14-17, 19, 22-25, 31 and 34 since the kit of Tomita et al contains the same physical components therein as the kit of the instant claims.

8. Claims 2-4 are allowable over the prior art of record since none of the prior art of record teaches of a method for detecting occult blood in a biological specimen by treating the specimen with sodium borohydride and monitoring the treated specimen for fluorescence.

9. Claims 8 and 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims for the same reasons as given above.

10. Applicant's arguments with respect to claims 1-19 and 22-35 have been considered but are moot in view of the new ground(s) of rejection.

The previous rejections of the claims under 35 USC 112, second paragraph made in the last Office action mailed on December 2, 2005 have been withdrawn in view of Applicants' amendments to the claims. A new rejection for claim 31 under this statute is set forth above. In addition, the previous rejections of the claims under 35 USC 102(a) and 35 USC 103 using the reference to Liu et al are withdrawn in view of the declaration under 37 CFR 1.132 filed February 1, 2006 that provides evidence that Liu et al does not qualify as prior art under 35 USC 102(a) since the Liu et al article was the sole work of the co-inventors of this application.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

February 21, 2006

Maureen M. Wallenhorst
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GROUP [redacted] 1700